REMARKS

The Office Action mailed December 30, 2005, has been carefully reviewed.

Claims 33, 37, and 47 have been amended and claims 49 – 52 added.

Claims 24 – 32 stand withdrawn as deemed to be allegedly directed to a non-elected invention.

Claims 33- 34, and 37 – 40 and 43-48 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent Publication 2004/0091500.

Claim 37 stands rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

Claim 47 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Applicants gratefully acknowledge telephonic conversation with the Examiner on February 13, 2006, and the Examiner's helpful suggestions.

The claims as amended herein are fully supported by the application as originally filed. No new matter has been added. Reconsideration and allowance of the present application are respectfully requested in view of the foregoing amendments and the following additional remarks which have addressed all the grounds for objection or rejection or otherwise have rendered them moot.

Claim Rejections under 35 U.S.C. § 112, first paragraph

Claim 37 stands rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Examiner suggested using "no allergenic activity" in lieu of "eliminated" allergenic activity.

Applicants welcome the Examiner's suggestion and have amended claim 37 accordingly. This rejection, thus obviated, it is respectfully requested that it be withdrawn.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claim 47 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner asserts that claim 47 does not further limit the base claim and is as such not a proper dependent claim.

Accordingly, the base claim has been amended and claim 47 has also been amended to further limit the base claim. This rejection, thus obviated, it is respectfully requested that it be withdrawn.

Claim Rejections under 35 U.S.C. § 102(e)

Claims 33- 34, and 37 – 40 and 43-48 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent Publication 2004/0091500 (herein after referred to as the "alleged prior art" or "Ipsen et al.") for reasons already of record. The Examiner asserts that the claims of the present invention are not drawn to inducing blocking antibodies but to methods of treatment by administering an allergen derivative that either induces IgG antibodies or has decreased IgE binding as compared to naturally occurring allergen.

Applicants have amended the claims such that they are now specifically directed to the administration of derivatives of naturally occurring allergens which induce IgE-blocking antibodies, **and conjunctively** have 50% or less allergenic activity compared to wild-type allergens.

In order for the alleged prior art to form the basis of a 35 U.S.C. § 102 rejection, every element of the claimed invention must be identically shown in a single reference. In re Bond, 910 F.2d 831, 15 USPQ2d 156 (Fed. Cir. 1990). To that extent, the alleged prior art does not teach an allergy treatment based on use of derivatives that induce IgE-blocking antibody production and conjunctively reduce IgE binding. Accordingly, this ground for rejection should now be withdrawn.

Applicants hereby reiterate the remarks previously made in connection with this alleged prior art in the response to the first office action. Since the claims are now drawn specifically to a method of using derivatives isolated solely on the basis of their IgE-blocking induction capability and substantially reduced allergenicity, said method not in any way taught or suggested by the prior art, Applicants submit that this ground for rejection is now obviated and the rejection should be withdrawn.

The Examiner appears to be arguing that the administration of any reduced IgE binding derivative such as that of the prior art which might have the incidental effect of inducing IgG production anticipates the claims of the present invention. Applicants vigorously disagree on the grounds that the Examiner's contention is not grounded in the sciences of the invention. The Examiner, in effect is, contending that the IgE epitopic sites always coincide with the IgG epitopic sites.

Essentially Ipsen et al. teaches the use of allergens that have an α-carbon backbone tertiary structure which is essentially the same as that of the natural allergen, thus ensuring conservation of the surface topology of areas surrounding conserved patches representing targets for mutagenesis aimed at reducing IgE binding. (Ipsen Paragraph 0048). The rationale behind Ipsen et al. is that point mutations are introduced in the Bet v 1 molecule without changing the overall fold of the protein in a relevant manner (see Figure 8) but in order to reduce the IgE binding of the protein. Ipsen et al. do not teach in any way the formulation of an allergy vaccine nor do they provide any example how a vaccine formulated with a mutated Bet v 1 would influence an existing IgE response in a host. Ipsen et al. do not provide any example of how the mutated proteins should be formulated as vaccines, or how

they should be administered and they also fail to provide any data that the mutated proteins induce IgE-blocking antibodies which can block IgE recognition of the wild type allergen. According to their description that the binding sites for IgE have been mutated, there is no evidence to believe that Ipsen's mutated protein can induce a blocking IgG response against an IgE epitope since the latter has been mutated.

Further, it should be stated that the application by Ipsen et al. does not differ in any relevant manner from prior art published by Takai et al., Smith et al., Burks et al., Ferreira et al. which are listed in paragraph 023 of the Ipsen application. Specifically the prior art by Ferreira is almost identical to the work described by Ipsen because it reports Bet v 1 mutant proteins which are characterized by a few amino acid exchanges, preserved T cell reactivity and reduced IgE reactivity.

The methodology of the present invention is based on the theory that allergen-specific IgG antibodies, termed blocking antibodies, can antagonize the cascade of allergic inflammation resulting from allergen recognition by IgE antibodies. The instant invention is based on the rationale that blocking antibodies inhibit allergen-induced release of inflammatory mediators from basophils and mast cells as well as IgE-facilitated allergen presentation to T cells, thus leading to suppression of T cell activation. Furthermore, the development of blocking antibodies is associated with reduced boosts of allergen-specific IgE production in patients receiving allergen-specific immunotherapy of the present invention. Thus blocking antibodies have protective activity by inhibiting immediate as well as late inflammatory responses and long-term ameliorating activity on the allergic immune response by antagonizing the underlying IgE production. Induction of blocking antibodies is thus an important mechanism underlying allergen-specific immunotherapy. See Specification pages 5 and 6.

As now distinctly claimed, a method of treatment using **derivatives** (not necessarily allergenic) capable of, **in vivo**, inducing IgG antibody production, while simultaneously inhibiting the binding of and or decreasing the production of allergen-specific IgE against naturally occurring allergens, are the derivatives of the present invention.

The methodology of the instant invention is simple, elegant and very effective. It does not concern itself with structural characterization of the allergen, nor the experimentally intensive structural conservation of the allergenic derivative, but instead chooses such derivatives, of whatever structural configuration, derived by substitution, fragmentation or any other means in the art, that is capable of inducing sufficient IgG production in vivo, such that the binding of allergen-specific IgE to the naturally occurring allergen is substantially reduced, if not totally eliminated.

Thus, while the alleged prior art involves the concept of dominant IgE binding epitopes and the therapeutic concept of initiating a new protective immune response (see paragraph 0030), the instant invention is concerned with the induction of IgG as "protective antibodies", ie antibodies which possibly prevent IgE from binding to the respective wild type protein from which the derivative is derived. See page 4.

Since the claims are now distinctly drawn to the use of derivatives that induce IgE-blocking antibody production, Applicants ask the Examiner to recognize that their method of treating allergic disorders is an elegant patentable departure from the experimentally intensive methodology of the alleged prior art. Applicants recognize that reduction or elimination of IgE binding is the ultimate therapeutic goal in the treatment of allergic disorders and that the complex patho-physiologic mechanisms of allergic response presents many therapeutic targets. Whereas the prior art taught IgE epitopic mapping and IgE epitopic manipulation of wild type allergens, it in no way concerned itself with IgG epitopic manipulation. The instant invention, on the other hand, and especially as now distinctly claimed, concerns itself with treatment using derivatives simply and quite elegantly identified by their ability to elicit IgE-blocking antibody production *in a test animal.* This method of treatment is in no way taught by or anticipated by the prior art. Applicants respectfully ask that this ground for rejection be withdrawn.

Regarding the newly added claims, support for them can be found on page 8 of the specification.

CONCLUSION

In view of the foregoing remarks, Applicants submit that there is no basis for applying the previous rejection to the pending claims and withdrawal of the rejections is respectfully requested. The claims are believed to be in condition for allowance, and Applicant earnestly solicits from the Examiner early notification of allowability.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, she is invited to contact the undersigned at his earliest convenience.

Respectfully submitted,

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